IUCLID

Data Set

Existing Chemical	:	ID: 61617-00-3
CAS No.	:	61617-00-3
EINECS Name	:	1,3-dihydro-4(or 5)-methyl-2H-benzimidazole-2-thione, zinc salt
EC No.	:	262-872-0
Molecular Formula	:	C8H8N2S.1/2Zn

Producer related part

Company	:	Epona Associates, LLC
Creation date	:	22.01.2004

Substance related part

Company	:	Epona Associates, LLC
Creation date	:	22.01.2004
Status	:	
Memo	:	RT Vanderbilt
Printing date	:	28.04.2006
Revision date	:	
Date of last update	:	28.04.2006
Number of pages	:	29
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	**:**	typical for marketed substance
Substance type	**:**	organometallic
Physical status	**:**	solid
Purity	**:**	= 95 - 97 % w/w
Colour	**:**	off-white to tan
Odour	**:**	
Source	**:**	RT Vanderbilt
Reliability	**:**	(1) valid without restriction

25.02.2004

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

Vanox® ZMTI

25.02.2004

Vulkanox® ZMB2/C5

Source **:** RT Vanderbilt
25.02.2004

Zinc mercaptotoluimidazole

25.02.2004

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	>= 700 °C
Sublimation	:	no
Method	:	other: Determination of melting point using Fisher-Johns melting point apparatus
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No decomposition
Source	:	RT Vanderbilt
Reliability	:	(2) valid with restrictions Acceptable study, but not GLP.
Flag	:	Critical study for SIDS endpoint

28.04.2006 (9)

2.2 BOILING POINT

Value	:	= 605 °C at 1013 hPa
Decomposition	:	
Method	:	other: Adapted Stein and Brown method
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Estimation method based on molecular structure and measured melting point value
Remark	:	Decomposition: no data
Reliability	:	(2) valid with restrictions Modelling data
Flag	:	Critical study for SIDS endpoint

25.02.2004 (5)

2.3 DENSITY

Type	:	
Value	:	= 1.69 g/cm³ at °C
Method	:	other: Determination of density of solids by pycnometry
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	RT Vanderbilt
Reliability	:	(2) valid with restrictions Methods other than pycnometry may be more reliable for determination of density of solids

25.02.2004 (8)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	= .0000000000001 hPa at 25 °C
Decomposition	:	
Method	:	other (calculated)
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	calculated, modified Grain method
Remark	:	Estimation method based on molecular structure and measured melting point value.
Result	:	4.64 x 10-14 mm Hg
Reliability	:	(2) valid with restrictions Modelling data
Flag	:	Critical study for SIDS endpoint

28.04.2006 (5)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= 3.07 at 20.5 °C
pH value	:	
Method	:	OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year	:	2004
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Shake Flask method OECD 107
Result	:	The partition coefficient is 1.17 x 10(3) at 20.5 +/- .5 deg C; log Pow is 3.07
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

05.05.2004 (20)

Partition coefficient	:	octanol-water
Log pow	:	= 3.06 at °C
pH value	:	
Method	:	other (calculated)
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	SRC LogKow (KowWin) Program
Remark	:	Estimation method based on molecular structure fragments
Source	:	RT Vanderbilt
Reliability	:	(2) valid with restrictions Modelling data

25.02.2004 (7)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= 32 mg/l at 20 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C

Description	:	
Stable	:	
Deg. product	:	
Method	:	OECD Guide-line 105
Year	:	
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method	:	OECD 105, OPPTS 830.7840
Source	:	RT Vanderbilt
Test substance	:	Purity ~ 95%
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

25.02.2004 (15)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	Sun light
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
DIRECT PHOTOLYSIS		
Halflife t1/2	:	= 1.2 hour(s)
Degradation	:	% after
Quantum yield	:	
INDIRECT PHOTOLYSIS		
Sensitizer	:	
Conc. of sensitizer	:	
Rate constant	:	= .000000000106 cm^3/(molecule*sec)
Degradation	:	% after
Deg. product	:	
Method	:	other (calculated)
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method : Atmospheric Oxidation Program/SAR Methods, 1995

Result : Direct photolysis:
Half life: 1.205 hours
Rate constant (radical): 106.4831x 10-12 cm3/molecule-sec
Rapid atmospheric degradation of test substance in vapor phase by reaction with photochemically produced hydroxyl radicals is expected. Particulate test substance may be physically removed from air by both wet and dry deposition. If released to air, test substance is expected to exist primarily in particulate phase.

Source : RT Vanderbilt

Reliability : (2) valid with restrictions
Modelling data.

28.04.2006 (3)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	at °C
t1/2 pH9	:	at °C
Deg. product	:	
Method	:	other: technical discussion
Year	:	2004
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Remark : VANOX® ZMTI antioxidant, is Zinc 2-mercaptotoluimidazole. The material is a water-insoluble zinc complex of 2-mercaptotoluimidazole. The material is not readily hydrolyzable, as it does not contain common hydrolysable organic functional groups such as carboxyl esters, nitriles and imines. Decomplexed, the free 2-mercaptotoluimidazole should also be resistant to hydrolysis, even though it is an imine-like material, due to the presence of a phenyl on the imine nitrogen.

Reliability : (2) valid with restrictions

28.04.2006 (16)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III
Media :
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: estimated
Year : 2004

Method : Fugacity level III
EPIWIN v3.10

Result : Level III Fugacity Model (Full-Output):
==========

Chem Name : 2H-Benzimidazole-2-thione, 1,3-dihydro-4(or 5)-methyl-, zinc sal (2:1)
Molecular Wt: 391.83
Henry's LC : 8.69e-015 atm-m3/mole (calc VP/Wsol)
Vapor Press : 1.4e-013 mm Hg (Mpbpwin program)
Liquid VP : 3.07e-011 mm Hg (super-cooled)
Melting Pt : 262 deg C (Mpbpwin program)
Log Kow : 3.06 (Kowwin program)
Soil Koc : 471 (calc by model)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.00222	2.41	1000
Water	17.5	1.44e+003	1000
Soil	82.1	1.44e+003	1000
Sediment	0.412	5.76e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	2.14e-018	29	1.01	0.967	0.0336
Water	8.79e-020	382	793	12.7	26.4
Soil	3.96e-019	1.79e+003	0	59.7	0
Sediment	8.42e-020	2.25	0.374	0.0749	0.0125

Persistence Time: 1.51e+003 hr
Reaction Time: 2.06e+003 hr
Advection Time: 5.71e+003 hr
Percent Reacted: 73.5
Percent Advected: 26.5

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 2.41
Water: 1440
Soil: 1440
Sediment: 5760
Biowin estimate: 2.075 (months)

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

Reliability : (2) valid with restrictions
Modelling data
Flag : Critical study for SIDS endpoint
28.04.2006 (2)

Type : adsorption
Media : other: soil/sediment
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: estimated
Year : 2003

Result : Koc = 3.22 x 103 ; Log Koc = 3.5081
Source : RT Vanderbilt
Reliability : (2) valid with restrictions
Modelling data
28.04.2006 (6)

Type : volatility
Media : other: water
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: estimated
Year : 2003

Remark : Model river = 1 m deep flowing at 1 m/sec and wind velocity of 5 m/sec. Model lake = 1 m deep flowing at 0.05 m/sec and wind velocity of 0.5 m/sec.
Result : Volatilization half-life from model river: 1.55 x1012 hours
Volatilization half-life from model lake: 1.691 x1013 hours
Source : RT Vanderbilt
Reliability : (2) valid with restrictions
Modelling data

28.04.2006 (4)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	domestic sewage, non-adapted
Contact time	:	
Degradation	:	= 27 (±) % after 28 day(s)
Result	:	other: not readily biodegradable but ultimately biodegradable
Deg. product	:	
Method	:	OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Year	:	
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	OECD 301B, EPA 835.3110 Concentration of the chemical: equivalent to 5 mg/l carbon Medium: defined culture mediu
Result	:	27% CO2 production after 28 days
Source	:	RT Vanderbilt
Test substance	:	Purity ~ 95%
Conclusion	:	not readily biodegradable but ultimately biodegradable
Reliability	:	(1) valid without restriction

28.04.2006 (14)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species	:	other: estimation
Exposure period	:	at °C
Concentration	:	
BCF	:	= 45.7
Elimination	:	
Method	:	other: calculated
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	RT Vanderbilt
Reliability	:	(2) valid with restrictions Modelling data

28.04.2006 (1)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	semistatic
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	= 2.1
LC50	:	= 5.6
Limit test	:	no
Analytical monitoring	:	yes
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	2003
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : Following a preliminary range-finding test, fish were exposed, in groups of 10, to solutions of the test material over a range of nominal concentrations of 0.67, 1.2, 2.1, 3.8, 6.7 and 12 mg/l for a period of 96 hours at a temperature of 13.0 to 14.4 deg C under semi-static conditions. The test material solutions were prepared by stirring an excess (150 mg/l) of test material in dechlorinated tap water at approximately 2000 rpm at a temperature of 25 deg C for 48 hours prior to removing any undissolved test material by filtration. A saturated solution with a nominal test concentration of 12 mg/l resulted, and was used to prepare the remainder of test concentrations through a series of dilutions. The number of mortalities and any sub-lethal effects of exposure in each test and control vessel were determined 3 and 6 hours after the start of exposure and then daily throughout the test until termination.

Result : The 96 hour LC50 based on nominal test concentrations was 5.6 mg/l with 95% confidence limits of 4.5 - 7.1 mg/L. The No Observed Effect Concentration was 2.1 mg/L. Analysis of test preparations at 0 (fresh media), 24, 48, 72 (old and fresh media) and 96 hours (old media) showed measured test concentrations to range frm 87% to 120% of nominal with the exception of the 1.2 mg/L test concentration at 0 hours which showed a measured concentration of 76% of nominal. This low measured concentation was considered to be due to sampling and/or analytical variation given that the corresponding 24-hour old test media sample showed a measured concentration of 93% of nominal value. It was considered justifiable to calculate the results based on nominal test concentrations only.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
28.04.2006 (18)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
NOEC	:	= .47
EC50	:	= 1.4

Limit Test	:	no
Analytical monitoring	:	yes
Method	:	OECD Guide-line 202
Year	:	2003
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : Following a preliminary range-finding test, 20 daphnids (2 replicates of 10 animals) were exposed to solutions of the test material over a range of nominal concentrations of 0.08, .14, .25, .45, .8, 1.4, 2.5, 4.5, and 8 mg/l for 48 hours at a temperature of ~21 deg C under static conditions. The nominal test concentrations were based on the results of chemical analysis of a saturated solution prepared for the pre-test recovery and stability analyses where the measured concentration of the saturated solution was 8 mg/l. The test material solutions were prepared by shaking an excess (150 mg/l) of test material in reconstituted water at approximately 300 rpm at a temperature of 30 deg C for 48 hours prior to cooling at 21 deg C and removing any undissolved test material by filtration. A saturated solution with a nominal test concentration of 12 mg/l resulted, and was used to prepare the remainder of test concentrations through a series of dilutions. The number of mortalities and any sub-lethal effects of exposure in each test and control vessel were determined 3 and 6 hours after the start of exposure and then daily throughout the test until termination. The number of immobilised daphnia were recorded after 24 and 48 hours.

Result : Chemical analysis of the saturated solution (also the top concentration) used to prepare the test concentrations at 0 hours showed a measured concentration of 15.7 mg/l (196% of the expected nominal value). As a consequence of this measured concentration in excess of the accepted 120% of nominal were observed for the test preparations at 0 and 48 hours. The nominal test concentrations assigned to the test were based on chemical analysis of a saturated solution prepared for the pre-test recovery and stability analysis. However, for the definitive test the saturated solution (also the top concentration) was determined to be 15.7 mg/l thereby resulting in significantly higher concentrations than the nominal concentrations assigned to the test. The measured concentration of the saturated solution (top concentration) was in-line with that obtained for the acute toxicity to rainbow trout test, which showed measured concentrations of approximately 13 mg/l. The difference between the measured concentration of the saturated solution prepared for the pre-test recovery and stability analysis and that prepared for the definitive test was considered to be possibly due to slight differences in preparation method despite efforts to maintain identical conditions between the two preparations.

Given that the measured concentrations were significantly in excess of the nominal concentrations assigned to the test it was considered acceptable to calculate the results based on the mean measured test concentration only.

The 48 hour EC50 based on the mean measured test concentration was 1.4 mg/l with 95% confidence limits of 1.1-1.6 mg/l and the No Observed Effect Concentration was 0.47 mg/l.

Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

28.04.2006 (17)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	biomass
Exposure period	:	72 hour(s)
Unit	:	mg/l
NOEC	:	= .69
EC50	:	= 6.6
Limit test	:	no
Analytical monitoring	:	yes
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	2003
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : Following a preliminary range-finding test Scenedesmus subspicatus was exposed to solutions of the test material over a range of nominal concentrations of 0.69, 1.38, 2.75, 5.5 and 11 mg/l (three replicate flasks per concentration) for 72 hours under constant illumination and shaking at a temperature of ~24 deg C. The test material solutions were prepared by shaking an excess (150 mg/l) of test material in culture medium at 300 rpm at a temperature of 30 deg C for 48 hours prior to removing any undissolved test material by filtration. A saturated solution with a nominal test concentration of 11 mg/l resulted, and was used to prepare the remainder of test concentrations through a series of dilutions. Samples of the algal populations were removed daily and cell concentrations determined for each control and treatment group.

Result : Exposure of Scenedesmus subspicatus to the test material gave an EbC50 (72 hour) value of 6.6 mg/l; 95% confidence limits of 5.8-7.5 mg/l and an ErC50 (0-72 hours) value of 10 mg/l. The No Observed Effect Concentration was .69 mg/l. Chemical analysis of the test solutions showed measured test concentrations to range from 85 to 96% of nominal and so it was considered justifiable to base the results on nominal test concentrations alone.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

28.04.2006 (19)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 800 mg/kg bw
Species	:	rat
Strain	:	Sherman
Sex	:	male
Number of animals	:	25
Vehicle	:	other: corn oil
Doses	:	0, 0.5, 1.0, 2.0, 4.0, 8.0 ml/kg b.w.
Method	:	other
Year	:	1977
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Test material was administered as a 25% w/v suspension in corn oil. Graded doses were administered to five groups of five male adult rats. The animals were observed for signs of toxicity and mortality for 14 days.
Result	:	At 4.0 ml/kg (1.0 g/kg) animals were severely depressed within 12 hours of dosing; at 8.0 ml/kg, all animals died within the first day. No abnormalities were observed in any test animal on necropsy. The LD50 was reported as 3.2 ml/kg with 19/20 Confidence Limits of from 2.5 to 4.3 ml/kg or 0.8 g/kg with 19/20 Confidence Limits of from 0.63 to 1.08 g/kg.
Source	:	RT Vanderbilt
Reliability	:	(2) valid with restrictions Acceptable study, but not GLP.
Flag	:	Critical study for SIDS endpoint

28.04.2006 (10)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	> 2.12 mg/l
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	0, 2.12 mg/l
Exposure time	:	4 hour(s)
Method	:	OECD Guide-line 403 "Acute Inhalation Toxicity"
Year	:	2003
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	OECD 403, OPPTS 870.1300 Test material was administered by nose-only exposure.
Result	:	Mass median aerodynamic diameter was 3.08 µ. There were no fatalities.
Test substance	:	Purity ~ 95%
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

28.04.2006 (11)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	> 2000 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	other: none; arachis oil used to moisten test article
Doses	:	2,000 mg/kg b.w.
Method	:	OECD Guide-line 402 "Acute dermal Toxicity"
Year	:	
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Test material was moistened with arachis oil and applied to an area of shorn skin. All test animals received a single dermal exposure of 2,000 mg/kg b.w. The test material was held in place by surgical gauze and self-adhesive bandage. The semi-occlusive wrap was removed after 24 hours and the excess material was wiped from the test animal.
Result	:	There were no deaths, no signs of systemic toxicity, no signs of dermal irritation and all animals showed expected weight gain. No abnormalities were noted at necropsy
Source	:	RT Vanderbilt
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

28.04.2006 (12)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	.5 g
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	slightly irritating
Classification	:	not irritating
Method	:	other: Draize, J.H., Woodard, G., and Calvery, H.O., 1944
Year	:	1977
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The skin on the dorsal surface of six animals was shaved with an electric clipper. The skin on one side of the animal was abraded with a lancet, sufficiently deep to penetrate the stratum corneum but not deep enough to cause bleeding. One-half (0.5) gram of test material was applied to each of two intact and two abraded sites on each animal. Test material was applied to the skin under gauze patches and held in contact with the skin by an occlusive wrap. The occlusive wrap

and gauze patches were removed after 24 hours. Treated areas were examined when test material was removed and 48 hours thereafter.

Result : Irritation was scored by the Draize Method; all scores were zero.
Test substance : Purity ~ 95%
Reliability : (2) valid with restrictions
Differs from current testing guidelines by using abraded skin surface, a 24-hr contact period rather than a 4-hr contact period.

28.04.2006 (10)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : undiluted
Dose : .1 other: g
Exposure time : 72 hour(s)
Comment : not rinsed
Number of animals : 6
Vehicle : none
Result : slightly irritating
Classification : not irritating
Method : other: Draize, J.H., Woodard, G., and Calvery, H.O., 1944
Year : 1977
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : One-tenth (0.1) gram test material was instilled into the conjunctival sac of the right eye of each animal; the left eye remained untreated as control. Test material was not washed from the eyes. Observations for signs of irritation were conducted one hour after application and 1, 2, 3, 5 and 7 days after dosing. The Draize Method was used for scoring eye irritation. The average Draize score for 24, 48 and 72 hours was calculated for each animal and then averaged over the six animals.
Result : The average Draize score was 0.3 on a scale from 0-110. All signs of irritation had subsided by the second day after exposure.
Source : RT Vanderbilt
Reliability : (1) valid without restriction
28.04.2006 (10)

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type : Sub-chronic
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : For 14 days prior to pairing, during mating, gestation and up to Day 5 of lactation for a total of 47 days
Frequency of treatm. : daily
Post exposure period : none
Doses : 1000, 2750 and 7500 ppm; reduced to 900, 2500 and 6750 ppm on Day 29; high dose level reduced to 5500 ppm on Day 33

Control group	:	yes
NOAEL	:	< 1000 ppm
Method	:	other: OECD 422
Year	:	2006
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : The test material was administered orally, by dietary inclusion, to groups of ten male and ten female rats throughout maturation, mating, gestation and up to Day 5 of lactation. The dose levels were 1000, 2750 and 7500 ppm of VANOX ZMTI in the diet. These dose levels were reduced to 900, 2500 and 6750 ppm, respectively, on study Day 29 to account for the anticipated increase in female food consumption during late gestation. On study day 33 the high dose level was further reduced to 5500 ppm as a result of the observed toxicity. A Control group of similar size was given untreated diet only. Following two weeks of dosing, male and female rats were paired within their dose groups to produce litters. At Day 5 post partum, all surviving females and offspring together with all adult males were killed and examined macroscopically. Parental animals were observed daily for clinical signs of toxicity. Bodyweights and food consumption were recorded weekly during the maturation phase, which was continued for males after the mating phase. On the day of initiation of treatment and on Days 8, 15 and 22, all animals were observed for signs of functional/behavioral toxicity. Functional performance tests (motor activity and forelimb/hindlimb grip strength) were also performed on five selected males and five selected females per group on Day 22 for males and Day 4 of lactation for females, together with an assessment of sensory reactivity to auditory, visual and proprioceptive stimuli. Mated females were weighed and food consumption recorded on specific days post coitum and post partum up to Day 5 of lactation. Blood sampling for haematology and clinical chemistry was performed on five selected males and five selected females per dose group one day prior to pairing. Post mortem macroscopic examinations were performed on all adults and offspring, including decedents. Selected reproductive organs testes, epididymides, ovaries) were weighed and/or preserved together with any significant abnormalities from all parental animals. In addition an extended list of organs/tissues (adrenals, brain, heart, kidneys, liver, spleen, and thymus) were weighed and/or preserved in fixative for selected males and females. Histopathology was carried out on specific organs from parental animals. Histopathology was also performed on the extended list of tissues preserved from selected males and females.

Result : There were a total of nine mortalities, which included, one high dose female and eight intermediate dose females. All these females were killed in extremis during late gestation. The majority of these mortalities were due to a possible impairment of the process of parturition.

There were clinical signs of reaction to treatment in high dose animals of either sex that were not indicative of behavioural toxicity.

Reductions in bodyweight gain and food consumption were seen throughout the treatment period for males and females when compared with controls.

Haematology of the high dose animals showed no significant trends despite the myeloid hypoplasia and splenic changes observed at histopathology. The clinical chemistry findings were indicative of alterations in metabolism including elevated cholesterol levels. Other blood chemistry changes including elevated plasma creatinine, phosphorus and chloride were not associated with renal changes at histopathology. The male absolute organ weight deficits were generally a consequence of lower bodyweight at termination with the exception of the liver where the relative organ weight was higher than controls. Of note were the reductions in

thymus and spleen weights. At histopathology treatment-related hypertrophy of the liver and thyroid glands were indicative of altered metabolism.

At the intermediate level there were similar clinical signs of reaction to treatment but at a lower incidence and frequency. Bodyweight gain and food consumption were reduced in a dosage related manner compared to other dose groups. Animals of the intermediate dose level showed similar haematological, blood chemical, organ weight changes and histopathological changes to that of the high dose level animals indicating a treatment and dosage related response. There were no mortalities or clinical signs of reaction to treatment in animals of either sex at the low dose level.

Reductions in bodyweight gain and food consumption were seen but at a lower rate than for higher dose levels. At clinical chemistry evaluation there were dosage related changes in plasma phosphorous, cholesterol and creatinine. Organ weight analysis showed similar changes in thymus and spleen weights as seen at higher dose levels.

The treatment-related histopathological changes seen in liver, thyroids and bone marrow of males were of note because of the dosage relationship and the nature of the changes seen.

Test substance : VANOX ZMTI; purity 99.9%
Conclusion : The administration of Vanox ZMTI to male and female rats at dose levels of up to 7500 ppm (adjusted to 6750 ppm and then to 5500 ppm) for a period of up to forty seven days; which included a mating period, gestation and early lactation phase, resulted in treatment-related toxic effects upon adults. The "No Observed Adverse Effect Level" (NOAEL) for general systemic effects upon adults was not established.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
28.04.2006 (22)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : Salmonella typhimurium TA1535, TA1537, TA102, TA98, TA100
Test concentration : 0, 50, 150, 500, 1500 and 5000 µg/plate
Cycotoxic concentr. : With metabolic activation: 5,000 µg/plate
Without metabolic activation: 5,000 µg/plate
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 471
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The test compound was evaluated for genetic activity in microbial assays with and without the addition of mammalian metabolic activation preparations. The Salmonella typhimurium strains used for this experiment were obtained from the University of California at Berkeley. The activation system used was S-9 homogenate from adult male Sprague-Dawley rat livers induced with phenobarbitone and ß-naphthoflavone. Positive controls for the non-activation assays were N-ethyl-N'-nitro-N-nitrosoguanidine, 9-aminoacridine, mitomycin C and 4-nitroquinoline-1-oxide. Positive control chemicals used for the activation assays were 2-aminoanthracine, benzo(a)pyrene, and

1.8-dihydroxyanthaquinone.

Result : Non-activation results: No mutagenic activity in any indicator organism at any dose.
Activation results: No mutagenic activity in any indicator organism at any dose.
A slight decrease in the frequency of revertant colonies was observed at the high dose.
Precipitate conc.: >5,000 µg/plate

Source : RT Vanderbilt
Test substance : Purity ~ 95%
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
28.04.2006 (13)

Type : Cytogenetic assay
System of testing : Human lymphocytes
Test concentration : preliminary toxicity test: 15.6 to 2000 ug/ml; Chromosome aberration test: 31.25, 62.5, 125, 250, 375, and 500 ug/ml
Cycotoxic concentr. : > 500 ug/ml
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 473
Year : 2005
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Duplicate cultures of human lymphocytes, treated with the test material, were evaluated for chromosome aberrations at up to three dose levels, together with vehicle and positive controls. Four treatment conditions were used for the study. In Experiment 1, 4 hours in the presence of an induced rat liver homogenate metabolizing system (S9), at a 2% final concentration with cell harvest after a 20-hour expression period and a 4 hour exposure in the absence of metabolic activation (S9) with a 20 hour expression period. In Experiment 2, the 4 hours exposure with addition of S9 was repeated (using a 1% final S9 concentration), while in the absence of metabolic activation the exposure time was increased to 24 hours.

Result : All vehicle (solvent) controls had frequencies of cells with aberrations within the range expected for normal human lymphocytes.

All the positive control materials induced statistically significant increases in the frequency of cells with aberrations indicating the satisfactory performance of the test and of the activity of the metabolizing system.

The test material was toxic and did not induce any statistically significant increases in the frequency of cells with aberrations, in either of two separate experiments, using a dose range that included a dose level that induced approximately 50% mitotic inhibition.

Test substance : Vanox® ZMTI
Conclusion : The test material did not induce any statistically significant increases in the frequency of cells with chromosome aberrations in either the absence or presence of a liver enzyme metabolizing system in either of two separate experiments. The test material was, therefore, considered to be non-clastogenic to human lymphocytes in vitro.
Reliability : (1) valid without restriction
28.01.2005 (21)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type	:	other: combined repeat dose toxicity study with reproduction/developmental screening test
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	For 14 days prior to pairing, during mating, gestation and up to Day 5 of lactation for a total of 47 days
Frequency of treatm.	:	daily
Premating exposure period		
Male	:	14 days
Female	:	14 days
Duration of test	:	Day 5 of lactation (up to 47 days)
No. of generation studies	:	2
Doses	:	1000, 2750 and 7500 ppm; reduced to 900, 2500 and 6750 ppm on study Day 29; high dose level reduced to 5500 ppm on study Day 33
Control group	:	yes
Method	:	OECD Guide-line 422
Year	:	2006
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : The test material was administered orally, by dietary inclusion, to groups of ten male and ten female rats throughout maturation, mating, gestation and up to Day 5 of lactation. The dose levels were 1000, 2750 and 7500 ppm of VANOX ZMTI in the diet. These dose levels were reduced to 900, 2500 and 6750 ppm, respectively, on study Day 29 to account for the anticipated increase in female food consumption during late gestation. On study day 33 the high dose level was further reduced to 5500 ppm as a result of the observed toxicity. A Control group of similar size was given untreated diet only. Following two weeks of dosing, male and female rats were paired within their dose groups to produce litters. At Day 5 post partum, all surviving females and offspring together with all adult males were killed and examined macroscopically.

In addition to the methodology previously described in section 5.4 for this study, the corpora lutea of all ovaries from pregnant females were counted at necropsy and uterine implantation sites were counted. The following parameters were calculated: pre-coital interval, mating index, pregnancy index, gestation length, parturition index, laive birth index, viability index, and sex ratio.

Result : Fertility: At the high dose level there was a marked reduction in the number of mating pairs with positive evidence of mating (four females mated). In addition, of those females with positive evidence of mating, only 50% achieved pregnancy (two females achieved pregnancy). The females with no evidence of mating generally showed a lack of oestrous cyclicity. Two of the mating pairs with positive evidence of mating also showed an increased pre-coital interval. These findings were considered to be of toxicological importance and treatment-related. At the intermediate and

low dose levels there were no treatment-related effects upon fertility. All mating pairs showed positive evidence mating and pregnancy.

Gestation and Parturition: At the high dose level one of the two pregnant females was killed due to possible dystocia. At the intermediate dose level eight females were killed in extremis during late gestation. The appearance of offspring, in utero in six of these females at post mortem examination was indicative of difficulties at parturition. Of the females that started delivery, there was an apparent increase in the gestation length. At the low dose level all females produced a live litter but there was a slight increase in the gestation lengths compared to controls.

Test substance : VANOX ZMTI; purity 99.9%
Conclusion : The administration of Vanox ZMTI to male and female rats at dose levels of up to 7500 ppm (adjusted to 6750 ppm and then to 5500ppm) for a period of up to forty seven days; which included a mating period, gestation and early lactation phase, resulted in treatment-related upon mating performance, fertility and the parturition process. The "No Observed Adverse Effect Level" (NOAEL) for reproductive effects upon adultswas not established.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
28.04.2006 (22)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : For 14 days prior to pairing, during mating, gestation and up to Day 5 of lactation for a total of 47 days
Frequency of treatm. : daily
Duration of test : up to lactation Day 5 for a total of 47 days
Doses : 1000, 2750 and 7500 ppm in the diet; reduced to 900, 2500 and 6750 ppm on study Day 29; high dose level reduced to 5500 ppm on study Day 33
Control group : yes
NOAEL teratogen. : = 1000 - ppm
Method : other: OECD 422
Year : 2006
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The test material was administered orally, by dietary inclusion, to groups of ten male and ten female rats throughout maturation, mating, gestation and up to Day 5 of lactation. The dose levels were 1000, 2750 and 7500 ppm of VANOX ZMTI in the diet. These dose levels were reduced to 900, 2500 and 6750 ppm, respectively, on study Day 29 to account for the anticipated increase in female food consumption during late gestation. On study day 33 the high dose level was further reduced to 5500 ppm as a result of the observed toxicity. A Control group of similar size was given untreated diet only. Following two weeks of dosing, male and female rats were paired within their dose groups to produce litters. At Day 5 post partum, all surviving females and offspring together with all adult males were killed and examined macroscopically.

In addition to the methodology previously described in section 5.4 for this study, individual offspring weights, number of live offspring and offspring sex were recorded on Days 1 and 4 post partum. The clinical condition of individual offspring was recorded daily.

Result : There were no significant clinical findings associated with live offspring

during the study. At the high and intermediate dose level, there were limited numbers of live litters to allow for meaningful evaluation of offspring weight gain. At the low dose level there were slightly lower live litter weights compared to control values but this did not attain statistical significance and was due to lower group mean litter sizes. Group mean individual offspring bodyweights were comparable with control values. At the high and intermediate dose group the limited number of live litters did not allow meaningful evaluation. At the low dose group there were no significant treatment-related differences in offspring sex ratios. At high and intermediate dose level there were limited numbers of offspring available for evaluation, but it is of note that the offspring of the intermediate dose level showed an increase in the number that had no milk in the stomach at examination. At the low dose level there were no significant findings.

Test substance : VANOX ZMTI; purity 99.9%
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
28.04.2006 (22)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

(1) BCFWIN v2.14

(2) EPISUITE/EPIWIN v3.10

(3) EPIWIN/AOPWIN v1.90

(4) EPIWIN/HYDROWIN v1.67

(5) EPIWIN/MPBPWIN v1.40

(6) EPIWIN/PCKOCWIN v1.66

(7) EPIWIN/WSKO v1.40

(8) R. T. Vanderbilt Standard Method of Analysis (T-288)

(9) R. T. Vanderbilt Standard Method of Analysis (T-3B)

(10) R. T. Vanderbilt study 06/07/1977

(11) R. T. Vanderbilt study 860-073

(12) R. T. Vanderbilt study 860-074

(13) R. T. Vanderbilt study 860-077

(14) R. T. Vanderbilt study 860-081

(15) R. T. Vanderbilt study 860/072

(16) RT Vanderbilt Company, Inc. (2004) Internal communication.

(17) SafePharm Laboratories (2003) Vanox ZMTI Acute Toxicity to Daphnia Magna SPL Project Number 860/079.

(18) SafePharm Laboratories (2003) Vanox ZMTI Acute Toxicity to Rainbow Trout (Oncorhynchus mykiss) SPL Project Number 860/078.

(19) SafePharm Laboratories (2003) Vanox ZMTI Algal Inhibition Test SPL Project Number 860/080.

(20) SafePharm Laboratories (2004) Vanox(R) ZMTI: Determination of Partition Coefficient. SPL Project Number: 860/114R

(21) SafePharm Laboratories (2005) Vanox ZMTI: Chromosome Aberration Test in Human Lymphocytes in Vitro. SPL Project Number 860/108.

(22) SafePharm Laboratories (2006) VANOX ZMTI: Dietary Combined Repeat Dose Toxicity Study with Reproduction/Developmental Screening Test in the Rat. SPL Project Number 860/076. March 15, 2006

10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT